

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: **Michael T. Migawa et al.** Confirmation No.: **2825**  
Serial No.: **10/592,919** Group Art Unit: **Not assigned**  
Filed: **9/15/2006** Examiner: **Not Assigned**  
Title: **COMPOSITIONS AND METHODS FOR OPTIMIZING CLEAVAGE  
OF RNA BY RNASE H**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

**PRELIMINARY AMENDMENT AND  
RESPONSE TO NOTICE OF DEFECTIVE RESPONSE**

In response to the Notification of Defective Response dated 2/5/2008 and preliminary to examination of the above-captioned patent application, please amend the application as follows:

- ☒ **Amendments to the Specification** begin on page 2 this paper.
- ☒ **Remarks/Arguments** begin on page 3 of this paper.

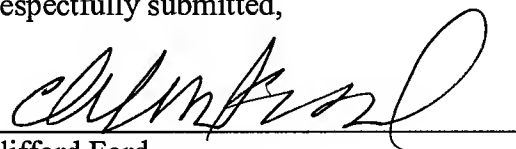
**IN THE APPLICATION:**

Please delete pages 1-12 of the Sequence Listing as filed and insert pages 1-12 of the Sequence Listing enclosed herewith.

**REMARKS**

The specification has been amended to include a substitute Sequence Listing which contains the nucleotide and/or amino acid sequences disclosed in the application. New pages 1-12 are provided to comply with the Sequence Rules set forth in 37 C.F.R. §§ 1.821-1.825. The Applicants submit that these amendments do not constitute new matter.

Respectfully submitted,



Clifford Ford

Registration No. 52,903

Date: 3/5/08

ISIS Pharmaceuticals, Inc.  
1896 Rutherford Rd.  
Carlsbad, CA 92008  
Telephone: (760) 931-9200  
Facsimile: (760) 603-3820